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EXAMINER	
HUYNH, PHUONG N	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 11/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/966,561	MILLER ET AL.	
	Examiner	Art Unit	
	Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 July 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *8-11 and 14-16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7, 12-13, and 17-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 1-23 are pending.

2. Claims 8-11 and 14-16 stand withdrawn from further consideration by the examiner, 37 C.F.R. 1.142(b) as being drawn to non-elected inventions.

3. In view of the amendment filed 7/17/03, the following objection and rejections remain.

4. The drawings, filed 9/27/01, stand not approved. Please see PTO 948, Notice of Draftsperson's Patent Drawing Review mailed 1/14/03. Appropriate action is required.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-7, 12-13, and 17-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for a method of making antibody that binds specifically to polypeptide comprising SEQ ID NO: 2 for a method of detecting hJIP1/IB1 of SEQ ID NO: 2 in CNS tissues, **does not** reasonably provide enablement for (1) a method of treating *any* neurological disorder in a human patient involving activation of c-Jun amino-terminal kinase 3 (JNK 3) which comprises administering to said human patient an effective amount of any polypeptide comprising any sequence "substantially equivalent" to SEQ ID NO: 2, or the polypeptide comprises the sequence depicted in SEQ ID NO: 2, (2) the said method wherein the polypeptide is administered in a composition further comprising a pharmaceutically acceptable carrier, (3) the said method wherein the polypeptide is administered intrathecally, (4) the said method is administered in conjunction with *any* other method of treating *any* neurological disorder, (5) the said method is caused by oxidative stress response in *any* neuronal tissue, (6) the said method wherein the neurological disorder is caused by the activation of *any* neuron specific, stress-activated protein kinase, (7) the said method wherein the neuron specific, stress-activated protein kinase is c-Jun amino-terminal kinase 3, (8) the said method wherein the polypeptide is administered in *any* targeted delivery system, any target delivery system such as liposome coated

with *any* antibody that specifically targets any neuronal tissue, (9) a method of treating a human subject for *any* neurological disease involving activation of c-Jun amino-terminal kinase 3 (JNK3) such as stroke, Alzheimer's disease, amyotrophic lateral sclerosis, age associated memory impairment and Parkinson's disease, the method comprising administering to said human an effective amount of *any* polypeptide "having a sequence that is *substantially equivalent*" to SEQ ID NO: 2, said polypeptide inhibit c-Jun phosphorylation by JNK3, (10) the method of treating a human subject for *any* neurological disease involving activation of c-Jun amino-terminal kinase 3 (JNK3) such as stroke, Alzheimer's disease, amyotrophic lateral sclerosis, age associated memory impairment and Parkinson's disease, the method comprising administering to said human an effective amount of *any* polypeptide "having a sequence that is *substantially equivalent*" to SEQ ID NO: 2, said polypeptide inhibit c-Jun phosphorylation by JNK3 wherein the polypeptide is administered in a composition further comprising a pharmaceutically acceptable carrier, (11) the method of treating a human subject for *any* neurological disease involving activation of c-Jun amino-terminal kinase 3 (JNK3) such as stroke, Alzheimer's disease, amyotrophic lateral sclerosis, age associated memory impairment and Parkinson's disease, the method comprising administering to said human an effective amount of *any* polypeptide "having a sequence that is *substantially equivalent*" to SEQ ID NO: 2, said polypeptide inhibit c-Jun phosphorylation by JNK3 is administered intrathecally, (12) the method of treating a human subject for *any* neurological disease involving activation of c-Jun amino-terminal kinase 3 (JNK3) such as stroke, Alzheimer's disease, amyotrophic lateral sclerosis, age associated memory impairment and Parkinson's disease, the method comprising administering to said human an effective amount of *any* polypeptide "having a sequence that is *substantially equivalent*" to SEQ ID NO: 2, said polypeptide inhibit c-Jun phosphorylation by JNK3 wherein the method is used in conjunction with any other method of treating stroke, (13) the method of treating a human subject for *any* neurological disease involving activation of c-Jun amino-terminal kinase 3 (JNK3) such as stroke, Alzheimer's disease, amyotrophic lateral sclerosis, age associated memory impairment and Parkinson's disease, the method comprising administering to said human an effective amount of *any* polypeptide "having a sequence that is *substantially equivalent*" to SEQ ID NO: 2, said polypeptide inhibit c-Jun phosphorylation by JNK3 wherein the polypeptide comprises the sequence depicted in SEQ ID NO: 2, (14) the method of treating a human subject for *any* neurological disease involving activation of c-Jun amino-terminal kinase 3 (JNK3) such as stroke, Alzheimer's disease, amyotrophic lateral sclerosis, age associated memory impairment and

Parkinson's disease, the method comprising administering to said human an effective amount of *any* polypeptide "having a sequence that is *substantially equivalent*" to SEQ ID NO: 2, said polypeptide inhibit c-Jun phosphorylation by JNK3 wherein the polypeptide comprises the sequence depicted in SEQ ID NO: 2, (15) A method of inhibiting apoptosis in human, comprising administering an effective of any polypeptide comprising any sequence that is "substantially equivalent" to SEQ ID NO: 2 to said human, said polypeptide effective to inhibit c-Jun phosphorylation by JNK3. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification discloses only polypeptide comprising SEQ ID NO: 2, which corresponding to human JIP-1/IB1 and a peptide consisting of SEQ ID NO: 3. The specification defines "substantially equivalent" as any mutant sequence that varies from a reference sequence by one more amino acid substitutions, deletions, or additions...no more than about 2% differences or 98% sequence identity to SEQ ID NO: 2 (See page 11 at lines 20-28). The specification further discloses a method of inhibiting c-Jun phosphorylation by JNK3 by administering polypeptide of SEQ ID NO: 2 in vitro (See page 31, Example 3), a method of generating antibody that binds to polypeptide of SEQ ID NO: 2 by immunizing rabbit a peptide consisting of SEQ ID NO: 3 for a method of detecting hJIP1/IB1 of SEQ ID NO: 2 in CNS tissues (page 31, Example 4). The specification further discloses that the antibody that binds to SEQ ID NO: 2 in human CA2 and CA3 regions of the normal hippocampus and the Purkinjie cells in the cerebellum (See page 32). With acute hypoxia, CA1 regions of the hippocampus show a major loss of staining of SEQ ID NO: 2, subiculum and Purkinkie cells (See Table 1). Under chronic hypoxic stress, there is a loss of cytoplasmic immunoreactivity of SEQ ID NO: 2 in Purkinjie cells. The decrease in SEQ ID NO: 2 staining in CA1 region of the hippocampus is

early as 2 hours. By 4 hours, there is a more extensive loss of SEQ ID NO: 2 staining in rat Hippocampal culture plus nuclear translocation of anti-DENN/MADD staining, and apoptosis as measured by anti-ssDNA (See page 35-36).

The specification does not teach how to make *any* sequence that is substantially equivalent to SEQ ID NO: 2 because there is no guidance as to which amino acid within the full-length sequence of SEQ ID NO: 2 can be substituted, deleted, added, mutated and whether the resulting sequence after substitution, deletion, addition would have the same functions as SEQ ID NO: 2. Even if the polypeptide is limited the sequence depicted in SEQ ID NO: 2, the specification does not teach a method of treating any neurological disorder such as stroke, let alone any neurological disorder such as the ones recited in claim 17. There is no in vivo working example demonstrating any sequence that is "substantially equivalent" to SEQ ID NO: 2 or sequence comprising SEQ ID NO: 2 can treat any neurological disorder, much less stroke for the following reasons.

Habgood *et al* teach most drugs produce their pharmacological response in a concentration-dependent manner and for a drug to be effective, it needs to reach and maintain a therapeutic concentration at its target site for sufficient time to exert its effect. Habgood et al further teach yet despite the availability of a large of number of very potent drugs, many central nervous system diseases and disorders remain extremely difficult to treat due to the inability of these drugs to penetrate into the brain (See page 231, in particular). A method of treating any neurological disease in the absence of in vivo working example is unpredictable because of the following reasons: 1) the polypeptide of SEQ ID NO: 2 or equivalent thereof having 711 amino acids in length has not been demonstrated to cross the blood brain barrier; (2) even if the polypeptide cross the blood brain barrier, there is no showing in the specification as filed that the polypeptide is capable of reaching to the neuronal cell within the CA1 region of the hippocampus or the Perkinjie cell is the in the cerebellum; (3) the polypeptide may be inactivated before producing an effect, i.e. such as proteolytic degradation, immunological inactivation or due to an inherently short half-life of the polypeptide or the polypeptide may be adsorbed by fluids, cells and tissues where the polypeptide has no effect; and (4) other functional properties, known or unknown, may make the polypeptide unsuitable for in vivo therapeutic use, i.e. such as adverse side effects of inflammation of the brain prohibitive to the use of such treatment. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

Given the indefinite number of undisclosed polypeptide comprising any sequence having substantially equivalent to polypeptide SEQ ID NO: 2, it is unpredictable which undisclosed sequence is effective and appropriate for treating any neurological disorder such as Alzheimer's disease, stroke, amyotrophic lateral sclerosis, age associated impairment, and Parkinson's disease, much less inhibiting apoptosis in the appropriate cells within the specific region of the brain that is affected by the specific neurological disorder. Even if the polypeptide is limited to SEQ ID NO: 2, there is no showing that the claimed polypeptide can actually inhibit apoptosis. Since the method of treating a neurological disorder using any sequence substantially equivalent to SEQ ID NO: 2 or SEQ ID NO: 2 is not enabled, it follows that method wherein the polypeptide is administered intrathecally in conjunction with another method is not enabled. It also follows that the method wherein neurological disorder is caused by oxidative stress response, in any neuronal tissue, or by the activation of a neuron specific stress activated protein kinase such as c-jun amino-terminal kinase 3 is not enabled.

For these reasons, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992). In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

Applicants' arguments filed 7/17/03 have been fully considered but are not found persuasive.

Applicants' position is that (1) claims 1, 3, 17, 19 and 21-23 have been amended. (2) modification of the polypeptide are taught at page 19, line 1 to page 20 line 25. (3) Applicants only need to teach one method of making and using the scope of the invention to meet the test of enablement. (3) Applicants teach intrathecal administration involving administration into the cerebrospinal fluid bathing the spinal cord and the brain. (3) Applicants teach that murine JIP-1 overexpression in PC-12 cells inhibits the NGF withdrawal-induced apoptosis of those cells (page 2, lines 18-19).

However, the breadth of the claims encompass treating any neurological disorder, any neurological disorder such as stroke, Alzheimer's disease, myotrophic lateral sclerosis, age

associated memory impairment or Parkinson's disease, Lou Gehrig's disease, dementia, dementia of the Alzheimer's type, bipolar disorders, mood disorder with depressive features, mood disorder with major depressive-like episode, mood disorder with manic features, mood disorder with mixed features, substance-induced mood disorder and mood disorder not otherwise specified (NOS), panic disorder without agoraphobia, panic disorder with agoraphobia, agorathobia without history of panic disorder, social phobia, posttraumatic stress disorder, acute stress disorder, substance-induced anxiety disorder and anxiety disorder not otherwise specified NOS, dyskinesias and behavioral manifestations of mental retardation, dementia selected from the group consisting of vascular dementia, dementia due to HIV disease, dementia due to head trauma, dementia due to Parkinson's disease, dementia due to Huntington's disease, dementia due to Pick's disease, dementia due to Creutzfeldt-lakob disease, substance-induced persisting dementia, dementia due to multiple etiologies and dementia not otherwise specified (NOS) in human patient using any polypeptide such as polypeptide comprising SEQ ID NO: 2 or any polypeptide substantially equivalent of SEQ ID NO: 2. The specification defines the term "substantially equivalent" can refer both to nucleotide and amino acid sequences, for example a mutant sequence, that varies from a reference sequence by one or more substitutions, deletions, or additions, the net effect of which does not result in an adverse functional dissimilarity between the reference and subject sequences. However, the specification does not teach which amino acid within SEQ ID NO: 2 can be substitute, delete or add and whether the resulting polypeptide has the same structure, much less about its function. Polypeptide comprising SEQ ID NO: 2 has 711 amino acids. A 2% difference is equivalent to 14 amino acid differences. Further, there is no in vivo working example demonstrating that treating any subject with any polypeptide such as polypeptide comprising SEQ ID NO: 2 or any substantially equivalent to SEQ ID NO: 2 is effective treating any neurological disorder mentioned above, much less all neurological disorder is mediated by JNK3. The specification merely discloses immunocytochemistry using anti-phospho-JNK antibody to detect JNK activation in rat organotypic hippocampal cultures before and after hypoxia. It is not clear that the reliance of immunocytochemistry in vitro using antibody that binds to SEQ ID NO: 2 correlates with the claimed method of treating any neurological disorder. Even if the polypeptide is administered intrathecally, there is no indication that the polypeptide goes to the right cell type such as the CA2, CA3 within the hippocampus in view of the fact that apoptosis is cell type and stimulus specific, much less inhibit c-Jun phosphorylation by JNK3 in vivo. In short, the specification does not provide any data of direct

therapeutic intervention of neurodegenerative diseases such as Alzheimer's disease using JNK inhibiting proteins.

7. Claims 1-7, 12-13, and 17-23 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** of (1) a method of treating *any* neurological disorder or *any* neurological disorder such as the ones recited in claims 8-9 and 17 in a human patient which comprises administering to said human patient an effective amount of any polypeptide comprising any sequence "substantially equivalent" to SEQ ID NO: 2, (2) the said method of treating *any* neurological disorder in a human patient which comprises administering to said human patient an effective amount of any polypeptide comprising any sequence "substantially equivalent" to SEQ ID NO: 2 wherein the polypeptide is administered in a composition further comprising a pharmaceutically acceptable carrier, (3) the method of treating *any* neurological disorder in a human patient which comprises administering to said human patient an effective amount of any polypeptide comprising any sequence "substantially equivalent" to SEQ ID NO: 2 wherein the polypeptide is administered orally, transdermally, intravenously, intrasynovially, intramuscularly, intraocularly, intranasally, intrathecally or topically, (4) the method of treating *any* neurological disorder in a human patient which comprises administering to said human patient an effective amount of any polypeptide comprising any sequence "substantially equivalent" to SEQ ID NO: 2 wherein the polypeptide is administered in conjunction with *any* other method of treating *any* neurological disorder, (5) the method of treating *any* neurological disorder in a human patient which comprises administering to said human patient an effective amount of any polypeptide comprising any sequence "substantially equivalent" to SEQ ID NO: 2 wherein the neurological disorder is caused by oxidative stress response in *any* neuronal tissue, (6) the method of treating *any* neurological disorder in a human patient which comprises administering to said human patient an effective amount of *any* polypeptide comprising *any* sequence "substantially equivalent" to SEQ ID NO: 2 wherein the neurological disorder is caused by the activation of *any* neuron specific, stress-activated protein kinase, (7) the method of treating *any* neurological disorder in a human patient which comprises administering to said human patient an effective amount of any polypeptide

comprising any sequence "substantially equivalent" to SEQ ID NO: 2 wherein the neuron specific, stress-activated protein kinase is c-Jun amino-terminal kinase 3, (8) the said method wherein the neurological disorder is caused by the activation of *any* neuron specific, stress-activated protein kinase wherein the polypeptide is administered in *any* targeted delivery system such as liposome coated with *any* antibody that specifically targets any neuronal tissue, (9) a method of treating a human subject for *any* neurological disease such as stroke, the method comprising administering to said human an effective amount of *any* polypeptide "having a sequence that is substantially equivalent" to SEQ ID NO: 2, (10) the method of treating a human subject for *any* neurological disease such as stroke, the method comprising administering to said human an effective amount of *any* polypeptide "having a sequence that is substantially equivalent" to SEQ ID NO: 2 wherein the polypeptide is administered in a composition further comprising a pharmaceutically acceptable carrier, (11) the method of treating a human subject for *any* neurological disease such as stroke, the method comprising administering to said human an effective amount of any polypeptide "having a sequence that is substantially equivalent" to SEQ ID NO: 2 wherein the polypeptide is administered orally, transdermally, intravenously, intrasynovially, intramuscularly, intraocularly, intranasally, intrathecally or topically, (12) the method of treating a human subject for *any* neurological disease such as stroke, the method comprising administering to said human an effective amount of any polypeptide "having a sequence that is substantially equivalent" to SEQ ID NO: 2 wherein the method is used in conjunction with any other method of treating stroke, (13) the method of treating *any* neurological disorder in a human patient which comprises administering to said human patient an effective amount of any polypeptide wherein the polypeptide has the sequence depicted in SEQ ID NO: 2, (14) the method of treating a human subject for *any* neurological disease such as stroke, the method comprising administering to said human an effective amount of any polypeptide wherein the polypeptide has the sequence depicted in SEQ ID NO: 2, (15) A method of inhibiting apoptosis in human, comprising administering an effective of any polypeptide "having any sequence that is substantially equivalent" to SEQ ID NO: 2 to said human.

The specification discloses only polypeptide comprising SEQ ID NO: 2, which corresponding to human JIP-1/IB1 and a peptide consisting of SEQ ID NO: 3. The specification defines "substantially equivalent" as any mutant sequence that varies from a reference sequence by one more amino acid substitutions, deletions, or additions...no more than about 2% differences or 98% sequence identity to SEQ ID NO: 2 (See page 11 at lines 20-28). The

specification further discloses a method of inhibiting c-Jun phosphorylation by JNK3 by administering polypeptide of SEQ ID NO: 2 in vitro (See page 31, Example 3), a method of generating antibody that binds to polypeptide of SEQ ID NO: 2 by immunizing rabbit a peptide consisting of SEQ ID NO: 3 for a method of detecting hJIP1/IB1 of SEQ ID NO: 2 in CNS tissues (page 31, Example 4). The specification further discloses that the antibody that binds to SEQ ID NO: 2 in human CA2 and CA3 regions of the normal hippocampus and the Purkinjie cells in the cerebellum (See page 32). With acute hypoxia, CA1 regions of the hippocampus show a major loss of staining of SEQ ID NO: 2, subiculum and Purkinkie cells (See Table 1). Under chronic hypoxic stress, there is a loss of cytoplasmic immunoreactivity of SEQ ID NO: 2 in Purkinjie cells. The decrease in SEQ ID NO: 2 staining in CA1 region of the hippocampus is early as 2 hours. By 4 hours, there is a more extensive loss of SEQ ID NO: 2 staining in rat Hippocampal culture plus nuclear translocation of anti-DENN/MADD staining, and apoptosis as measured by anti-ssDNA (See page 35-36).

With the exception of the specific polypeptide comprising SEQ ID NO: 2, there is insufficient written description about the structure of any polypeptide comprising any sequence "substantially equivalent" to SEQ ID NO: 2, much less having the same function as SEQ ID NO: 2, in turn, for a method of treating *any* neurological disorder such as stroke in a human patient.

Further, given the lack of a written description of *any* additional representative species of polypeptide comprising a sequence substantially equivalent to SEQ ID NO: 2 for detection assay, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.*

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicants' arguments filed 7/17/03 have been fully considered but are not found persuasive.

Applicants' position is that (1) The claims have been amended to clarify that the disease, disorder or apoptosis be one that is mediated by JNK3. (2) the written description requires only that an application reasonably convey to one of skill in the art that the inventors were in possession of the invention at the time of filing.

However, the breadth of the claims encompass treating any neurological disorder, any neurological disorder such as Alzheimer's disease, stroke, myotrophic lateral sclerosis, age associated memory impairment or Parkinson's disease, Lou Gehrig's disease, dementia, dementia of the Alzheimer's type, bipolar disorders, mood disorder with depressive features, mood disorder with major depressive-like episode, mood disorder with manic features, mood disorder with mixed features, substance-induced mood disorder and mood disorder not otherwise specified (NOS), panic disorder without agoraphobia, panic disorder with agoraphobia, agorathobia without history of panic disorder, social phobia, posttraumatic stress disorder, acute stress disorder, substance-induced anxiety disorder and anxiety disorder not otherwise specified NOS, dyskinesias and behavioral manifestations of mental retardation, dementia selected from the group consisting of vascular dementia, dementia due to HIV disease, dementia due to head trauma, dementia due to Parkinson's disease, dementia due to Huntington's disease, dementia due to Pick's disease, dementia due to Creutzfeldt-lakob disease, substance-induced persisting dementia, dementia due to multiple etiologies and dementia not otherwise specified (NOS) in human patient using any polypeptide such as polypeptide comprising SEQ ID NO: 2 or any polypeptide substantially equivalent of SEQ ID NO: 2. The specification defines the term "substantially equivalent" can refer both to nucleotide and amino acid sequences, for example a mutant sequence, that varies from a reference sequence by one or more substitutions, deletions, or additions, the net effect of which does not result in an adverse functional dissimilarity between the reference and subject sequences. However, the specification does not teach which amino acid within SEQ ID NO: 2 can be substitute, delete or add and whether the resulting polypeptide has the same structure, much less about its function. Polypeptide comprising SEQ ID NO: 2 has 711 amino acids. A 2% difference is equivalent to 14 amino acid differences. Further, there is no in vivo working example demonstrating that treating any subject with any polypeptide such as polypeptide comprising SEQ ID NO: 2 or any substantially equivalent to SEQ ID NO: 2 is effective treating any neurological disorder mentioned above, much less all neurological disorder is mediated by JNK3. The specification merely discloses immunocytochemistry using anti-phospho-JNK antibody to detect JNK activation in rat organotypic hippocampal cultures before and after hypoxia. It is not clear that the reliance of immunocytochemistry in vitro using antibody that binds to SEQ ID NO: 2 correlates with the claimed method of treating any neurological disorder. Even if the polypeptide is administered intrathecally, there is no indication that the polypeptide goes to the right cell type such as the CA2, CA3 within the hippocampus in

view of the fact that apoptosis is cell type and stimulus specific, in addition to the transient nature of the kinase phosphorylation. In short, the specification does not provide any in vivo data of direct therapeutic intervention of neurodegenerative diseases such as stroke, Alzheimer's disease using JNK inhibiting proteins. The specification discloses only one polypeptide comprising SEQ ID NO: 2. Given the lack of a written description of *any* additional representative species of polypeptide comprising a sequence "substantially equivalent" to SEQ ID NO: 2 as encompassed by the claims for a method of treating any neurological disorder, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.*

8. No claim is allowed.

9. **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to "Neon" Phuong Huynh whose telephone number is (703) 308-4844. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

11. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

Phuong N. Huynh, Ph.D.
Patent Examiner
Technology Center 1600
November 17, 2003

Christina Chan

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600